REMARKS

Claims 1-3 are pending and have been amended.

At the outset the undersigned thanks Examiner Patel for the courtesy shown during the telephone interview held May 12, 2004. On the basis of that interview and this Amendment applicant is hopeful that the subject application is now in condition for allowance.

Applicant acknowledges with appreciation the determination that the claimed invention is patentable over DE 3720317 (Nussbaumer, et al.).

CLAIMS ARE NOT INDEFINITE

The rejection of claim 1 under 35 U.S.C. §112, second paragraph, has been maintained. This rejection is respectfully traversed.

The rejection was based on the recitation of "A biologically active agent" in the preamble claim 1. Although applicant disagrees with the basis of the rejection, in order to advance prosecution the preamble of claim 1 has been amended to recite a "compound" as recommended in the March 25, 2004 Office Action. Dependent claims 2-3 have been amended to conform to the amendment of claim 1.

Support for the claims as amended may be found, *inter alia,* in the claims as originally filed. Applicant maintains that the amendment does not introduce new matter. The original preamble did not limit the claims. It neither recited essential structure or steps, nor was it necessary to give life, meaning and vitality to the claim, nor did applicant rely on the preamble to distinguish the claimed invention from the prior art. See Catalina

Mktg. Int'l, Inc. v. Coolsavings.com, Inc., 289 F.3d 801, 808, 62 USPQ.2d 1781, ____ (Fed. Cir. 2002).

Applicant respectfully submits that the amendment overcomes the rejection under Section 112, second paragraph.

CLAIMED INVENTION IS NOVEL

Claims 1-3 have been rejected under 35 U.S.C. 102(b) as allegedly being anticipated by WO 97/17317 (Giordani). This rejection is respectfully traversed.

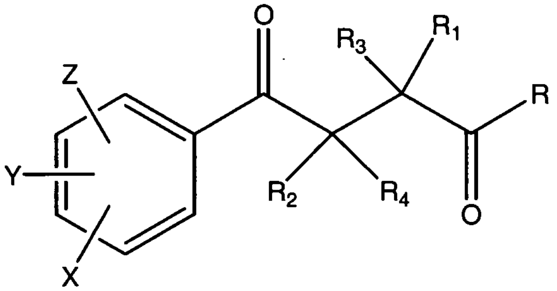
The Giordani reference discloses a genus of 4-phenyl-4-oxobutanoic acid derivatives encompassing more than a trillion (10^{12}) compounds. The Giordani genus is written in Markush format utilizing multiple variables. It generically encompasses the compounds claimed by applicant, and one could arrive at the claimed compounds by selecting certain values for variable substituents from a large number of possibilities. In none of the compounds preferred by or exemplified in the reference is the phenyl ring di-substituted at the 2- and 6- positions.

The claimed compounds have been rejected based on two generic formulas in Giordani. The rejection stated:

> Giordani teaches making of Compounds of Formula IV (see pages 13, 15) and Compounds of Claim 1, Formula (I) (see page 44). . . . The reference compounds have a core:," Halogenated-phenyl-CO-CR2R4-CR3R1-CO-R wherein R is OH, R1, R2, R3, R4 are H, and Y is H/alkyl, and Z/X can be fluorines as claimed herein.

Office Action, page 2. Contrary to the assertion of the rejection, no selection of variables for Formula IV of Giordani will result in the compounds claimed by applicant. Formula IV of Giordani (pages 13 and 15) contains a double bond that is not present in the claimed compounds. "Anticipation of a patent claim requires a finding that the claim at issue 'reads on' a prior art reference." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1346, 51 USPQ.2d 1943, ____ (Fed. Cir. 1999). Formula IV of the reference does not even read on the compounds recited in the claims of the subject application, much less disclose any of them.

With regard to Formula I of Giordani, the passage cited in the rejection defines a genus of 4-phenyl-4-oxobutanoic acid derivatives as follows:



> wherein
>
> X, Y and Z are, each independently, hydrogen, halogen, cyano, nitro, C_1-C_6 alkyl, phenyl, benzyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_1-C_6 alkoxy or C_1-C_6 alkylthio;
>
> R is hydroxyl; OR_5 in which R_5 is C_1-C_6 alkyl, phenyl, benzyl, C_2-C_4 alkenyl or C_2-C_4 alkynyl; $-N(R_6)_2$ or $-N(R_6)OR_6$ in which each R_6 is, independently, hydrogen, C_1-C_6 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, phenyl or benzyl;
>
> R_1, R_2, R_3 and R_4 are, each independently, hydrogen, halogen, hydroxyl, thiol, C_1-C_6 alkoxy, C_1-C_6 alkylthio, C_1-C_6 alkyl, C_2-C_4 alkenyl, phenyl or benzyl, or
>
> R_1 and R_3 or R_2 and R_4 together form a group $=CHR_8$ in which R_8 is hydrogen, a straight C_1-C_5 alkyl chain or phenyl. . . .

Giordani, page 44.

The above-quoted passage from the reference generically encompasses more than a trillion (10^{12}) compounds. In none of the Formula I compounds preferred by or exemplified in the reference is the phenyl ring substituted at the 2- and 6- positions, let alone 2,6-difluoro substituted. To the extent that preferences can be discerned from Giordani, the preferred substitution sites are the 3- and 4- positions (Giordani, claim 10, pages 46-47). Moreover, when the phenyl ring is di-substituted with fluorine, Giordani prefers that "R_1, R_2, R_3 and R_4 are not simultaneously hydrogen" (Page 8, line 8 to page 9, line 15, especially page 8, lines 23-24). Referring to the nomenclature used in the reference, the claims of the subject application are directed to the compounds in which R is hydroxyl or -OR_5 in which R_5 is C_1-C_6 alkyl; R_1, R_2, R_3 and R_4 are all hydrogen; one of X,Y and Z is hydrogen and the other two are fluoro and are located at the 2-position and the 6-position, respectively, of the phenyl ring.

As a general rule, the disclosure in a prior art reference of a generic formula does not anticipate a species that is encompassed by that generic formula. This can be seen from the decision of the CCPA in In re Ruschig. In Ruschig the Board had found claims directed to certain sulfonylurea compounds to be anticipated by the disclosure in the prior art of a genus that encompassed the claimed compounds. In reversing the anticipation rejection the CCPA stated:

> "We hold similar views as to the board's indication that a specific description of compounds within claims 1 and 2 can be made out of the Martin disclosure. To do this the board selects p-chloro- and p-bromo- for R (as used in appellants' claim 2, supra) and ethyl or isoamyl for R(2) to create, ex post facto, four undisclosed specific compounds out of a possible 259, according to appellants' apparently valid calculations. This is not the kind of description we found in Petering, and we do not find here any 'anticipation' by the Martin patent of claims 1 and 2."

In re Ruschig, 52 CCPA 1238, 1251, 343 F.2d 965, 974-5, 145 USPQ 274, ____ (1965) (Ruschig I). As seen from the above-quoted passage the court in Ruschig found that a genus encompassing 259 compounds did not anticipate four specific compounds encompassed by the genus.

A limited exception to the general rule of Ruschig can be found in situations where the genus is so small that one can "at once envisage" each of its members. The prevailing jurisprudence considers Petering to have "involved a very special situation" (In re Ruschig, 343 F.2d 965, 973, 145 USPQ 274 (CCPA 1965) (Ruschig I)) in which what was special included "the disclosure of a small genus" of twenty compounds (Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc., 246 F.3d 1368, 1380, 58 USPQ.2d 1508 (Fed. Cir. 2001)) and "the description of specific preferences" for the variables (Merck & Co., Inc. v. Biocraft Laboratories, Inc., 874 F.2d 804, 807, 10 USPQ.2d 1843 (Fed. Cir. 1989)). The importance of a small genus, after taking into account any preferences described in the prior art reference, is intimately related to the rationale of Petering. In Petering the court concluded that the person of ordinary skill in the art upon reading the prior art patent would, "at once envisage each member of this limited class." In re Petering, 301 F.2d 676, 681, 133 USPQ 275, ___ (CCPA 1962). Only with a small genus can one "at once envisage" each of its members.

The reference discloses a genus encompassing more than a trillion (10^{12}) compounds. No teaching in the reference points toward substitution with fluorine at the 2- and 6-positions. This is not the special situation in which the rule of In re Petering was intended to apply. Accordingly, the claims are not anticipated under 35 U.S.C. §102.

THE OBVIOUSNESS REJECTIONS

The Office Action mentions two different references, WO 97/17317 (Giordani) and WO 95/05376 (Berryman, et al.), in connection with the alleged obviousness of the claimed invention. From the text of the Office Action itself it is unclear whether Berryman forms the basis of a separate obviousness rejection or if Berryman is being cited as a secondary reference in combination with Giordani. During the May 11, 2004 telephone conference Examiner Patel advised the undersigned to explain how the claimed invention is nonobvious over the references, either separately or in combination. Applicant does so in the following three sections, first addressing each of the references separately and then in combination.

INVENTION IS NONOBVIOUS OVER WO 97/17317

Claims 1-3 have been rejected under 35 USC §103(a) as allegedly being obvious over WO 97/17317 (Giordani). This rejection is respectfully traversed.

The Giordani reference is the same reference that is used for the anticipation rejection discussed above. As discussed above, Giordani discloses a genus of 4-phenyl-4-oxobutanoic acid derivatives encompassing more than a trillion (10^{12}) compounds.

"The fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious." In re Baird, 16 F.3d 380, 382, 29 USPQ2d 1550, ____ (Fed. Cir. 1994), citing In re Jones, 958 F.2d 347, 350, 21 USPQ2d 1941, 1943 (Fed. Cir. 1992). The decision of the CCPA in In re Susi (440 F.2d 442, 169 USPQ 423 (CCPA 1971)) cited in the Office Action, is not to the contrary. In Susi the obviousness rejection was upheld not solely because the prior art genus of compounds overlapped with the applicant's compounds, but also because the prior art genus was "of a class of chemicals to be used for the same purpose" as the applicant's compounds (In re Susi, at 445). In this case the Giordani compounds are said to be useful in the prevention and treatment of certain neurodegenerative diseases, in contrast to the uses disclosed in the specification of the subject application (Specification, page 8, lines 19-27).

The rejection is also based on an improper "obvious to try" standard. Thus the Office Action states:

> It would have been obvious . . . to . . . make various combinations . . . and try out the use/utility as a pharmaceutical by using the conventional chemistry knowledge. The motivation stems from the expectation of making compounds having equal or better pharmaceutical agent.

Office Action, page 3 (underlining added). This "obvious to try" approach is an insufficient basis for an obviousness rejection. A general motivation to search for a compound having desirable properties does not render obvious the specific compound that is ultimately obtained. In re Deuel, 51 F.3d 1552, 1558, 34 USPQ2d 1210, ____ (Fed. Cir. 1995) ("A general motivation to search for some gene that exists does not necessarily make obvious a specifically-defined gene that is subsequently obtained as a result of that search.")

Certainly, one could arrive at the claimed compounds by selecting certain values for variable substituents from a large number of possibilities, if one knew which values to select. But Giordani does nothing to simplify the "needle in a haystack"-like task of picking and choosing such variables from a large number of possibilities to arrive at the claimed compounds.

In attempting to find a teaching based on Giordani that would guide the skilled artisan to the claimed invention, the rejection looks to examples of dihalogenated compounds in the reference. The rejection stated:

> Giordani differs from the instant compounds by claiming dihalogenated as well as polyhalogenated compounds and their use as pharmaceuticals.
>
> It would have been obvious to . . . prepare instant compounds by modifying or replacing hydrogen atom of phenyl ring by fluorine atoms and make various combinations as 2,6-difluro [sic], 2,4-difluor [sic] and others to prepare the 2,6-difluorocompound of a benzene derivative. . . .

(Office Action, page 3). Indeed, Giordani discloses a number of dihalogenated compounds (pages 5, 8 and 9), but in every case the halogens are located at the 3- and 4-positions, not at the 2- and 6-positions. Moreover, when the phenyl ring is di-substituted with a halo group, Giordani prefers that "R_1, R_2, R_3 and R_4 are not simultaneously hydrogen" (Giordani, page 8, lines 20-24). Far from suggesting the making of compounds that are 2,6-difluoro-substituted and in which R_1, R_2, R_3 and R_4 are all hydrogen, Giordani's preferences, if anything, lead away from such compounds.

In view of the foregoing, applicant respectfully submits that this rejection is improper and should be withdrawn.

INVENTION IS NONOBVIOUS OVER WO 95/05376

Claims 1-3 have been rejected under 35 USC §103(a) as allegedly being obvious over WO 95/05376 (Berryman, et al.). A full-length copy of the Berryman reference is enclosed. This rejection is respectfully traversed.

The rejection is based, in part, on the incorrect allegation that a specific compound disclosed by Berryman has pharmaceutical activity. The rejection states:

> Berryman. . . teaches a final compound with CAS RN #169803-96-7 with a core:"2,6-difluorophenyl-CO-CH2-CH (COOMe)-1,3-Benzodioxole".
>
> * * *
>
> It would have been obvious . . . to prepare instant compounds by modifying or replacing the Benzodioxole ring . . . by H atom . . . and try out the use/utility as a pharmaceutical . . . . The motivation stems from the expectation of making compounds having equal or better pharmaceutical agent [sic].

Office Action, paragraph 10, pages 3-4 (underlining added). The reference compound differs from the claimed compounds in having a 1,3-benzodioxole substituent at the 2-position of the butyric acid moiety. Contrary to the above-quoted passage from the rejection, Berryman does not disclose any pharmaceutical activity for the reference compound. Rather, it is a member of a genus of compounds that is used as a synthetic intermediate (Berryman, pages 48-49). Accordingly, even if presented with the claimed compounds, based on Berryman the person of ordinary skill in the art would not have expected such compounds to have pharmaceutical activity just as the reference compound is not disclosed to have any pharmaceutical activity. Therefore, there was no motivation to make the claimed compounds.

The rejection is also based on the incorrect assertion that Berryman discloses a genus that encompasses the compounds claimed by applicant. Thus the rejection states:

> It has been held that a prior art disclosed compounds [sic] is sufficient to render a prima facie case of obviousness as [sic] species falling within a genus. See In re SUSI, 440 F 2d 442, 169 USPQ 423, 425 (CCPA 1971), followed by Federal Circuit in Merck & co. [sic] V. [sic] Biocraft Laboratories, 847 F 2d 804, 10 USPQ 2d 1843, 1846 (Fed. Cir. 1989).

Office Action, paragraph 11, page 4. Contrary to the implication of the above-quoted passage, the claimed compounds are not encompassed by any genus disclosed by Berryman. Berryman discloses a genus of furanone compounds which are said to have a number of therapeutic uses. Berryman teaches a synthetic approach that utilizes a genus of intermediates of which the reference compound is an example (Berryman, pages 48-49 and 173) For the Berryman genus of intermediates to encompass the claimed compounds, R_1 would have to be hydrogen. However hydrogen is not one of the possible values for R_1 (Berryman, page 12, lines 12-20; and page 49). Therefore no teaching of Berryman is related to the claimed invention as genus to species.

As noted above, R_1 cannot be hydrogen in Berryman. Accordingly, if the claimed compounds were substituted for the genus of intermediates disclosed in reaction Scheme I of Berryman, the resulting compound would not be one of the compounds disclosed by Berryman to have pharmaceutical activity. Therefore there was no motivation to make the claimed compounds based on Berryman.

The rejection is based on an improper "obvious to try" standard. Thus the Office Action states:

> It would have been obvious . . . to prepare instant compounds by modifying or replacing the Benzodioxole ring of the chain/bridge (= -CH-ring/cycle) by H atom and make various combinations of 2,6-difluro [sic] methyl or alkyl esters and try out the use/utility as a pharmaceutical by using the conventional chemistry knowledge. The motivation stems from the expectation of making compounds having equal or better pharmaceutical agent.

Office Action, page 3 (underlining added). This "obvious to try" approach is an insufficient basis for an obviousness rejection. A general motivation to search for a compound having desirable properties does not render obvious the specific compound that is ultimately obtained. In re Deuel, 51 F.3d 1552, 1558, 34 USPQ2d 1210, ____ (Fed. Cir. 1995) ("A general motivation to search for some gene that exists does not necessarily make obvious a specifically-defined gene that is subsequently obtained as a result of that search.")

In view of the foregoing, applicant respectfully submits that this rejection is improper and should be withdrawn.

INVENTION IS NONOBVIOUS OVER WO 97/17317 AND WO 95/05376

Claims 1-3 have been rejected under 35 USC §103(a) as allegedly being obvious over WO 97/17317 (Giordani) in combination with WO 95/05376 (Berryman). This rejection is respectfully traversed. The teachings of the references are discussed above.

To reject an invention based on a combination of references the PTO has the burden of demonstrating that the person of ordinary skill in the art would have been motivated to combine the relevant teachings of the references. That motivation cannot be based on an applicant's specification. As stated by the Federal Circuit:

> The PTO has the burden under section 103 to establish a *prima facie* case of obviousness. It can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to one of

> ordinary skill in the art would lead that individual to combine the relevant teachings of the references.

In re Fine, 837 F.2d 1071, 1074, 5 USPQ2d 1596, ____ (Fed. Cir. 1988). In this case the Office has pointed to nothing in the art or the knowledge of the person of ordinary skill that would have lead one to select those portions of the references in such way as to arrive at applicant's invention.

The Giordani reference discloses a genus of 4-phenyl-4-oxobutanoic acid derivatives encompassing more than a trillion (10^{12}) compounds. It generically encompasses the compounds claimed by applicant, and one could arrive at the claimed compounds by selecting certain values for variable substituents from a large number of possibilities. Berryman discloses a genus of intermediate compounds that overlaps with Giordani. However the subset of compounds that is included in both Giordani and Berryman excludes the claimed compounds. Therefore, even if one were motivated to combine the references, the combination would lead away from the claimed compounds.

Berryman also discloses a specific intermediate compound (CAS RN #169803-96-7) which has a 2-6-difluoro-substituted phenyl ring like the claimed compounds, but which differs from the claimed compounds in having an extra 1,3-benzodioxole substituent. Changing the 1,3-benzodioxole group to hydrogen would yield one of the claimed compounds and would also yield a compound encompassed by the Giordani genus. But, absent the disclosure of the subject invention, the person of ordinary skill in the art would not have been motivated to do so with any reasonable expectation of success for reasons including the following:

Because the Berryman compound has no disclosed pharmaceutical activity itself and is used only as an intermediate for synthesizing compounds very different from the Giordani compounds, the person of ordinary skill would not have looked to Berryman for guidance as to which values to select for the variables X, Y, Z, R, R_1, R_2, R_3 and R_4 from among the numerous possibilities encompassed by the Giordani genus.

Likewise, because the Giordani genus is different structurally from the furanone compounds that are disclosed by Berryman to have pharmaceutical activity, Giordani would not have guided the person of ordinary skill to modify the Berryman genus of furanone compounds by allowing hydrogen as a possible value of R_1 in Berryman. Without a motivation to make the furanone-based pharmaceutically-active compounds in which R_1 is hydrogen, there would have been no reason to make the corresponding intermediate compounds in which R_1 is hydrogen.

Nothing in the combined teaching of Giordani and Berryman would have motivated the person of ordinary skill in the art to make the claimed invention. Accordingly, applicant respectfully maintains that the rejection is improper and should be withdrawn.

REQUEST TO WITHDRAW FINALITY OF REJECTION

Applicant requests that the finality of the May 10, 2004 rejection be withdrawn as premature. May 10, 2004 Office Action contains several art rejections, all of which are new. The new rejections cannot have been necessitated by an amendment of applicant because the application was not amended in response to the first Office Action. Moreover, the new rejections cannot have been necessitated by an information disclosure statement (IDS) under 37 CFR 1.97(c) because applicant did not submit such an IDS. In accordance with Office procedure, an Office Action containing such rejections should not be made final. MPEP 706.07(a), 8th ed., Rev. 1, Feb. 2003.

The finality of the rejection was discussed during the May 11, 2004 telephone conference. During the telephone conference the Examiner stated that he would not withdraw the finality of the rejection, but that he would make every effort to ensure that amendments presented by applicant would be entered. In the event that the subject application is not deemed to be in condition for allowance, s would respectfully request that the finality of the May 10, 2004 Office Action be withdrawn and a further action on the merits be issued so that any remaining issues can be fully developed.

CONCLUSION

Reconsideration of all objections and rejections is respectfully requested. Applicant believes that the subject application is in condition for allowance and looks forward to a favorable action.

It is believed that no fee is required in connection with the filing of this Amendment. If any fee is required, the Commissioner is hereby authorized to charge the amount of such fee to Deposit Account No. 50-1677.

Respectfully submitted,

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Enclosure: WO 95/05376 (Berryman, et al.)